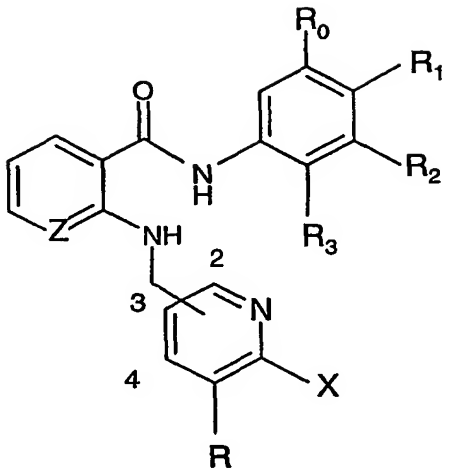
Claims:

1. An anthranilic acid amide of formula I,



(I)

wherein

R and R_0 represent H, halogen,

alkynyl, alkenyl, alkyl, which in each case is unsubstituted or substituted by halogen;

unsubstituted or substituted mono- or bicyclic aryl;

unsubstituted or substituted mono- or bicyclic heteroaryl having 1 to 3 heteroatoms selected from O, N or S;

unsubstituted or substituted heterocyclyl having at least one N atom;

mono- or dialkyl amino, wherein the alkyl radical is unsubstituted or substituted by unsubstituted or substituted aryl, unsubstituted or substituted mono- or bicyclic heteroaryl having 1 to 3 heteroatoms selected from O, N or S or substituted by unsubstituted or substituted heterocyclyl having at least one N atom;

unsubstituted or substituted heterocyclyl carbonyl alkyl amino, wherein the heterocyclyl radical comprises at least one N atom;

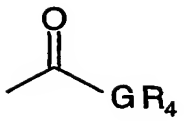
R_1 represents H, halogen, unsubstituted or substituted C_{1-7}alkyl, C_{2-7}alkenyl, C_{2-7}alkynyl, alkoxy or a radical

$-O-(CH_2)_n-CF_3$, wherein n is 0, 1, 2 or 3,

R_2 is perfluoro alkyl,

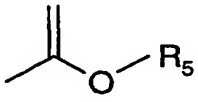
R_3 represents H or halogen,

X represents hydroxy, alkoxy, alkyl thio, imino, alkyl imino, halogen, a radical of formula I'



(I')

wherein G is CH_2 or NH and R_4 is hydrogen, alkyl or aryl, or a radical of formula I"



(I")

wherein R_5 is alkyl or aryl,

Z is N or CH, and

wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 2-, 3-, 4- or 5-position,

under the proviso that R cannot represent H, if Z is nitrogen, X is hydroxy or methoxy and wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 3-position, and R_1 and R_3 cannot both represent H if Z is CH, R represents H, X is hydroxy, alkoxy or alkyl thio and wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 3-position,

or an N-oxide or a tautomer thereof,

or a salt of such anthranilic acid amide, its N-oxide or its tautomer.

2. An anthranilic acid amide of formula I according to claim 1, wherein

R represents H, halogen,

alkynyl, alkenyl, alkyl, which in each case is unsubstituted or substituted by halogen;

unsubstituted or substituted mono- or bicyclic aryl;

unsubstituted or substituted mono- or bicyclic heteroaryl having 1 to 3 heteroatoms selected from O, N or S;

unsubstituted or substituted heterocyclyl having at least one N atom;

mono- or dialkyl amino, wherein the alkyl radical is unsubstituted or substituted by unsubstituted or substituted aryl, unsubstituted or substituted mono- or bicyclic heteroaryl having 1 to 3 heteroatoms selected from O, N or S or substituted by unsubstituted or substituted heterocyclyl having at least one N atom;

unsubstituted or substituted heterocyclyl carbonyl alkyl amino, wherein the heterocyclyl radical comprises at least one N atom;

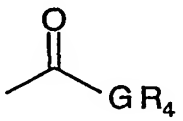
R_0 represents H,

R_1 represents H, halogen, C_{2-7}alkyl, C_{2-7}alkenyl, C_{2-7}alkynyl, alkoxy or a radical $-O-(CH_2)_n-CF_3$, wherein n is 0, 1, 2 or 3,

R_2 is perfluoro alkyl,

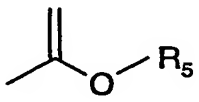
R_3 represents H or halogen,

X represents hydroxy, alkoxy, alkyl thio, imino, alkyl imino, halogen, a radical of formula I'



(I')

wherein G is CH_2 or NH and R_4 is hydrogen, alkyl or aryl, or a radical of formula I"



(I")

wherein R_5 is alkyl or aryl,

Z is N or CH, and

wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 2-, 3-, 4- or 5-position,

under the proviso that R cannot represent H, if Z is nitrogen, X is hydroxy or methoxy and wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 3-position, and R_1 and R_3 cannot both represent H if Z is CH, R represents H, X is hydroxy, alkoxy or alkyl thio and wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 3-position,

or an N-oxide or a tautomer thereof,

or a salt of such anthranilic acid amide, its N-oxide or its tautomer.

3. An anthranilic acid amide of formula I according to claim 1

wherein

R represents H, halogen, alkenyl, alkyl, pyridyl alkyl amino, morpholinyl alkyl amino, alkyl piperazinyl alkyl amino, alkyl piperazinyl carbonyl alkyl amino, phenyl alkyl amino, alkyl

amino, thienyl, pyridyl, furanyl, thiazolyl, naphthyl or phenyl which is unsubstituted or substituted by trifluoromethyl, phenyl, alkanoyl or alkanoyl amino,

R_1 represents H, halogen, C_{2-7}alkyl, C_{2-7}alkenyl, C_{2-7}alkynyl, alkoxy or a radical $-O-(CH_2)_n-CF_3$, wherein n is 0, 1, 2 or 3,

R_2 is perfluoro alkyl,

R_3 represents H or halogen,

X represents hydroxy, alkoxy, alkyl thio, imino, alkyl imino, halogen, a radical of formula I' wherein G is CH_2 or NH and R_4 is hydrogen or alkyl, or a radical of formula I" wherein R_5 is alkyl,

Z is N or CH, and

wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 2-, 3-, 4- or 5-position,

under the proviso that R cannot represent H, if Z is nitrogen, X is hydroxy or methoxy and wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 3-position, and R_1 and R_3 cannot both represent H if Z is CH, R represents H, X is hydroxy, alkoxy or alkyl thio and wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 3-position,

or an N-oxide or a tautomer thereof,

or a salt of such anthranilic acid amide, its N-oxide or its tautomer.

4. An anthranilic acid amide of formula I according to claim 1, wherein

R represents H, halogen, lower alkenyl, lower alkyl, pyridyl lower alkyl amino, morpholinyl lower alkyl amino, lower alkyl piperazinyl lower alkyl amino, lower alkyl piperazinyl carbonyl lower alkyl amino, phenyl lower alkyl amino, lower alkyl amino, thienyl, pyridyl, furanyl, thiazolyl, naphthyl or phenyl which is unsubstituted or substituted by trifluoromethyl, phenyl, lower alkanoyl or lower alkanoyl amino,

R_1 represents H, halogen, C_{2-7}alkyl, C_{2-7}alkenyl, C_{2-7}alkynyl, lower alkoxy or a radical $-O-(CH_2)_n-CF_3$, wherein n is 0, 1, 2 or 3,

R_2 is trifluoromethyl,

R_3 represents H or halogen,

X represents hydroxy, lower alkoxy, lower alkyl thio, imino, lower alkyl imino, halogen, a radical of formula I' wherein G is CH_2 or NH and R_4 is hydrogen or lower alkyl, or a radical of formula I" wherein R_5 is lower alkyl,

Z is N or CH, and

wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 2-, 3-, 4- or 5-position,

under the proviso that R cannot represent H, if Z is nitrogen, X is hydroxy or methoxy and wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 3-position, and R_1 and R_3 cannot both represent H if Z is CH, R represents H, X is hydroxy, lower alkoxy or lower alkyl thio and wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 3-position,

or an N-oxide or a tautomer thereof,

or a salt of such anthranilic acid amide, its N-oxide or its tautomer.

5. An anthranilic acid amide of formula I according to claim 1, wherein

R represents H, halogen, lower alkenyl, lower alkyl, pyridyl lower alkyl amino, morpholinyl lower alkyl amino, lower alkyl piperazinyl lower alkyl amino, lower alkyl piperazinyl carbonyl lower alkyl amino, phenyl lower alkyl amino, lower alkyl amino, thienyl, pyridyl, furanyl, thiazolyl, naphthyl or phenyl which is unsubstituted or substituted by trifluoromethyl, phenyl, lower alkanoyl or lower alkanoyl amino,

R_1 represents H, halogen, C_{2-7}alkyl, C_{2-7}alkenyl, C_{2-7}alkynyl, lower alkoxy or a radical $-O-(CH_2)_n-CF_3$, wherein n is 0 or 1,

R_2 is trifluoromethyl,

R_3 represents H or halogen,

X represents hydroxy, lower alkoxy, halogen,

a radical of formula I' wherein R_4 is hydrogen or lower alkyl, or

a radical of formula I" wherein R_5 is lower alkyl,

Z is N or CH, and

wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 3- or 4-position,

under the proviso that R cannot represent H, if Z is nitrogen, X is hydroxy or methoxy and wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 3-position, and R_1 and R_3 cannot both represent H if Z is CH, R represents H, X is hydroxy, lower alkoxy or lower alkyl thio and wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 3-position,

or an N-oxide or a tautomer thereof,

or a salt of such anthranilic acid amide, its N-oxide or its tautomer.

6. An anthranilic acid amide of formula I according to claim 1, wherein

R represents H, halogen, lower alkenyl, lower alkyl, pyridyl lower alkyl amino, morpholinyl lower alkyl amino, lower alkyl piperazinyl lower alkyl amino, lower alkyl piperazinyl carbonyl lower alkyl amino, phenyl lower alkyl amino, lower alkyl amino, thienyl, pyridyl, furanyl, thiazolyl, naphthyl or phenyl which is unsubstituted or substituted by trifluoromethyl, phenyl, lower alkanoyl or lower alkanoyl amino,

R_1 represents H, halogen, C_{2-7}alkyl, or C_{2-7}alkynyl,

R_2 is trifluoromethyl,

R_3 represents H or halogen,

X represents hydroxy, lower alkoxy, halogen,

a radical of formula I' wherein R_4 is hydrogen or lower alkyl, or

a radical of formula I" wherein R_5 is lower alkyl,

Z is CH, and

wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 3- or 4-position,

under the proviso that R_1 and R_3 cannot both represent H in compounds of formula I wherein R represents H, X is hydroxy, lower alkoxy or lower alkyl thio and wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 3-position,

or an N-oxide or a tautomer thereof,

or a salt of such anthranilic acid amide, its N-oxide or its tautomer.

7. An anthranilic acid amide of formula I according to claim 1, wherein

R represents H, halogen, allyl, 3-methyl-buten-2-yl, propyl, ethylamino, pyridylethylamino, morpholinylethylamino, N-methyl-piperazinylpropylamino, N-methyl-piperazinylethylamino, N-methyl-piperazinylacetylamino, benzylamino, thienyl, pyridyl, furanyl, thiazolyl, naphthyl or phenyl which is unsubstituted or substituted by trifluoromethyl, phenyl, formyl or acetylamino,

R_1 represents H, halogen, propyl, propynyl,

R_2 is trifluoromethyl,

R_3 represents H or halogen,

X represents hydroxy, lower alkoxy, halogen,
a radical of formula I' wherein R_4 is hydrogen or lower alkyl, or
a radical of formula I" wherein R_5 is lower alkyl,
Z is CH, and
wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 3- or 4-position,
under the proviso that R_1 and R_3 cannot both represent H in compounds of formula I wherein R represents H, X is hydroxy, lower alkoxy or lower alkyl thio and wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 3-position,
or an N-oxide or a tautomer thereof,
or a salt of such anthranilic acid amide, its N-oxide or its tautomer.

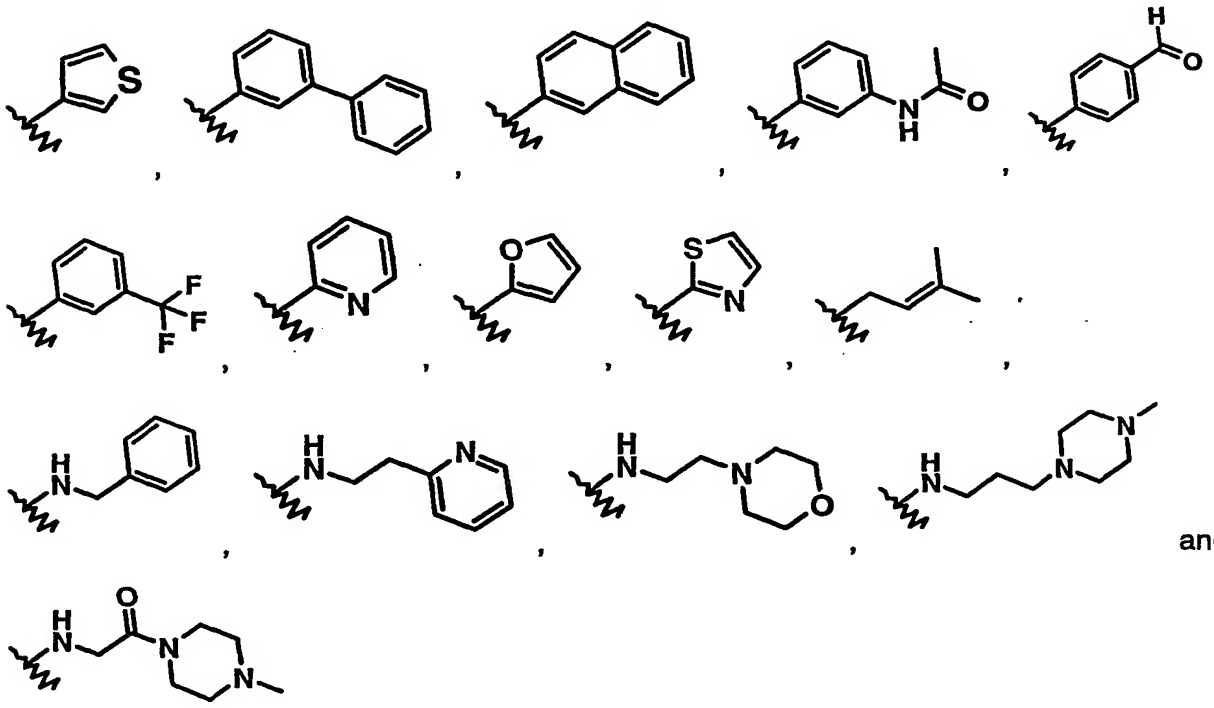
8. An anthranilic acid amide of formula I according to claim 1, wherein
R represents halogen, lower alkenyl, lower alkyl, pyridyl lower alkyl amino, morpholinyl lower alkyl amino, lower alkyl piperazinyl lower alkyl amino, lower alkyl piperazinyl carbonyl lower alkyl amino, phenyl lower alkyl amino, lower alkyl amino, thienyl, pyridyl, furanyl, thiazolyl, naphthyl or phenyl which is unsubstituted or substituted by trifluoromethyl, phenyl, lower alkanoyl or lower alkanoyl amino,
R_1 represents H,
R_2 is trifluoromethyl,
R_3 represents H,
X represents hydroxy or lower alkoxy,
Z is CH, and
wherein the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 3- or 4-position,
or an N-oxide or a tautomer thereof,
or a salt of such anthranilic acid amide, its N-oxide or its tautomer.

9. An anthranilic acid amide of formula I according to claim 1 selected from
2-[[6-Methoxy-3-pyridinyl]methyl]amino-*N*-[4-bromo-3-(trifluoromethyl)phenyl]benzamide,
2-[[2-Bromo-4-pyridinyl]methyl]amino-*N*-[(3-trifluoromethyl)phenyl)benzamide,
2-[[6-Methoxy-4-pyridinyl]methyl]amino-*N*-[3-(trifluoromethyl)phenyl]benzamide,
2-[[6-Methoxy-3-pyridinyl]methyl]amino-*N*-[2-fluoro-3-(trifluoromethyl)phenyl]benzamide,

2-[[6-Methoxy-3-pyridinyl]methyl]amino-*N*-[4-chloro-3-(trifluoromethyl)phenyl]benzamide,
2-[[6-Methoxy-3-pyridinyl]methyl]amino-*N*-[4-(1-propynyl)-3-(trifluoromethyl)phenyl]-benzamide,
2-[[6-Methoxy-3-pyridinyl]methyl]amino-*N*-[4-(1-propyl)-3-(trifluoromethyl)phenyl]benzamide hydrochloride salt,
2-[[(1,6-Dihydro-6-oxo-3-pyridinyl)methyl]amino]-*N*-[4-propynyl-3-(trifluoro-methyl)phenyl]benzamide,
2-[[(1,6-Dihydro-6-oxo-3-pyridinyl)methyl]amino]-*N*-[4-propyl-3-(trifluoromethyl)-phenyl]benzamide,
2-[[(1,6-Dihydro-6-oxo-3-pyridinyl)methyl]amino]-*N*-[2-fluoro-3-(trifluoromethyl)-phenyl]benzamide,
2-[[(1,6-Dihydro-6-oxo-3-pyridinyl)methyl]amino]-*N*-[4-chloro-3-(trifluoromethyl)-phenyl]benzamide,
2-[[2-(1-Ethoxyethenyl)-4-pyridinyl]methyl]amino-*N*-[(3-trifluoromethyl)phenyl)benzamide,
2-[(2-Acetyl-4-pyridinyl)methyl]amino-*N*-[(3-trifluoromethyl)phenyl)benzamide,
2-[[(1,6-Dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-(2,2,2-trifluoroethoxy)-3-(trifluoromethyl)phenyl]benzamide,
2-[[(1,6-Dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[2-fluoro-4-(2,2,2-trifluoroethoxy)-3-(trifluoromethyl)phenyl]benzamide,
2-[[(1,6-Dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-(2,2,2-trifluoropropoxy)-3-(trifluoromethyl)phenyl]benzamide,
2-[[(1,6-Dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-trifluoromethoxy)-3-(trifluoromethyl)phenyl]benzamide,
2-[[(1,6-Dihydro-6-oxo-3-pyridinyl)methyl]amino]-N-[4-(2,2,2-trifluoroethoxy)-3-(trifluoromethyl)phenyl]nicotinamide,
2-[[6-Methoxy-3-pyridinyl]methyl]amino-*N*-[4-fluoro-3-(trifluoromethyl)phenyl]benzamide,
2-[[(1,6-Dihydro-6-oxo-3-pyridinyl)methyl]amino]-*N*-[4-fluoro-3-(trifluoromethyl)-phenyl]benzamide,
2-[(5-Bromo-6-methoxy-pyridin-3-ylmethyl)-amino]-N-(3-trifluoromethyl-phenyl)-benzamide,
2-[[(1,6-Dihydro-5-bromo-6-oxo-3-pyridinyl)methyl]amino]-*N*-[3-(trifluoromethyl)-phenyl]benzamide,
2-[(6-Methoxy-5-phenyl-pyridin-3-ylmethyl)-amino]-N-(3-trifluoromethyl-phenyl)-benzamide,
2-[(6-Oxo-5-phenyl-1,6-dihydro-pyridin-3-ylmethyl)-amino]-N-(3-trifluoromethyl-phenyl)-benzamide,

2-[(5-Allyl-6-methoxy-pyridin-3-ylmethyl)-amino]-N-(3-trifluoromethyl-phenyl)-benzamide,
2-[(5-^{n}Propyl-6-methoxy-pyridin-3-ylmethyl)-amino]-N-(3-trifluoromethyl-phenyl)-benzamide,
2-[(5-Allyl-6-oxo-1,6-dihydro-pyridin-3-ylmethyl)-amino]-N-(3-trifluoromethyl-phenyl)-benzamide,
2-[(5-^{n}Propyl-6-oxo-1,6-dihydro-pyridin-3-ylmethyl)-amino]-N-(3-trifluoromethyl-phenyl)-benzamide,
2-[(5-Ethylamino-6-methoxy-pyridin-3-ylmethyl)-amino]-N-(3-trifluoromethyl-phenyl)-benzamide,
2-[(5-Ethylamino-6-oxo-1,6-dihydro-pyridin-3-ylmethyl)-amino]-N-(3-trifluoromethyl-phenyl)-benzamide,
2-({5-[2-(4-Methyl-piperazin-1-yl)-ethylamino]-6-oxo-1,6-dihydro-pyridin-3-ylmethyl}-amino)-N-(3-trifluoromethyl-phenyl)-benzamide,
2-({6-Methoxy-5-[2-(4-methyl-piperazin-1-yl)-ethylamino]-pyridin-3-ylmethyl}-amino)-N-(3-trifluoromethyl-phenyl)-benzamide,
2-({5-[2-(4-Methyl-piperazin-1-yl)-ethylamino]-6-oxo-1,6-dihydro-pyridin-3-ylmethyl}-amino)-N-(3-trifluoromethyl-phenyl)-benzamide,
2-{[(1,6-Dihydro-6-oxo-3-pyridinyl)methyl]amino}-*N*-(4-methyl-3-trifluoromethyl-phenyl)benzamide,
2-{[(1,6-Dihydro-6-oxo-3-pyridinyl)methyl]amino}-*N*-[3-(4-ethyl-piperazin-1-ylmethyl)-5-trifluoromethyl-phenyl]benzamide,
2-{[(1,6-Dihydro-6-oxo-3-pyridinyl)methyl]amino}-*N*-[3-(azetidin-1-ylmethyl)-5-trifluoromethyl-phenyl]benzamide,
2-[(6-Methoxy-3-pyridinyl)methyl]amino-*N*-[4-(4-methyl-piperazin-1-ylmethyl)-3-trifluoromethyl-phenyl]benzamide,
2-{[(1,6-Dihydro-6-oxo-3-pyridinyl)methyl]amino}-*N*-[4-(4-methyl-piperazin-1-ylmethyl)-3-trifluoromethyl-phenyl]benzamide,
2-{[(1,6-Dihydro-6-oxo-3-pyridinyl)methyl]amino}-*N*-4-[[2-(dimethylamino)ethyl]methylamino]-3-trifluoromethyl-phenyl]benzamide, and
2-{[(1,6-Dihydro-6-oxo-3-pyridinyl)methyl]amino}-*N*-5-(5-Methyl-1H-imidazol-1-yl)-3-trifluoromethyl-phenyl]benzamide,
or a tautomer thereof,
or a salt of such anthranilic acid amide or its tautomer.

10. An anthranilic acid amide of formula I according to claim 1 wherein
R_1 and R_3 are H, R_2 is CF_3, Z is CH, X is OH or OMe,
the methylen group is attached to the pyridyl moiety at the carbon atom of the pyridyl moiety in 3-position and
R is a radical selected from the following group:



and

11. An anthranilic acid amide of formula I according to any one of claims 1 to 10, or an N-oxide or a tautomer thereof, or a pharmaceutically acceptable salt of such a compound, for use in a method for the treatment of the human or animal body.

12. Use of an anthranilic acid amide of formula I according to any one of claims 1 to 10, or an N-oxide or a tautomer thereof, or a pharmaceutically acceptable salt of such a compound, for the preparation of a pharmaceutical product for the treatment of a neoplastic disease.

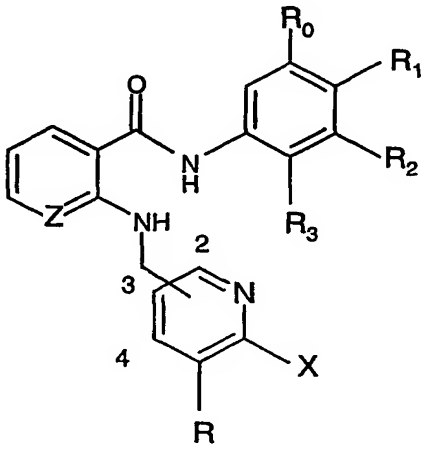
13. Use of an anthranilic acid amide of formula I, according to any one of claims 1 to 10, or an N-oxide or a tautomer thereof, or a pharmaceutically acceptable salt of such a

compound, for the preparation of a pharmaceutical product for the treatment of retinopathy or age-related macula degeneration.

14. A method for the treatment of a neoplastic disease which responds to an inhibition of the VEGF-receptor tyrosine kinase activity, which comprises administering an anthranilic acid amide of formula I according to any one of claims 1 to 10, or a N-oxide or a tautomer thereof, or a pharmaceutically acceptable salt of such anthranilic acid amide, its N-oxide or its tautomer, in a quantity effective against said disease, to a warm-blooded animal requiring such treatment.

15. A pharmaceutical preparation, comprising an anthranilic acid amide of formula I according to any one of claims 1 to 10, or an N-oxide or a tautomer thereof, or a pharmaceutically acceptable salt of such a compound, or a hydrate or solvate thereof, and at least one pharmaceutically acceptable carrier.

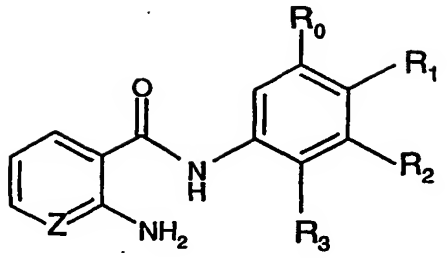
16. A process for the preparation of an anthranilic acid amide of formula I



(I)

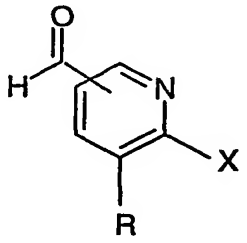
wherein X represents lower alkoxy, lower alkylthio, lower alkylimino or halogen and the remaining symbols R, R_0, R_1, R_2, R_3 and Z are as defined in claim 1 for a compound of the formula I,

wherein a compound of the formula II



(II)

wherein R_0, R_1, R_2, R_3 and Z are as defined for a compound of the formula I, is reacted with a carbonyl compound of the formula III



(III)

wherein X represents lower alkoxy, lower alkylthio, lower alkylimino or halogen and R is as defined for a compound of the formula I, in the presence of a reducing agent,

wherein the starting compounds of formula II and III may also be present with functional groups in protected form if necessary and/or in the form of salts, provided a salt-forming group is present and the reaction in salt form is possible;

wherein any protecting groups in a protected derivative of a compound of the formula I are removed; and, if so desired, an obtainable compound of formula I is converted into another compound of formula I or a N-oxide thereof, a free compound of formula I is converted into a salt, an obtainable salt of a compound of formula I is converted into the free compound or another salt.